CLAIMS

We hereby claim:

1. A method of identifying a ligand which can mediate the biological activity of a target protein via inhibition of the binding of a target protein to a binding partner which comprises

(a) screening a first combinatorial library comprising a plurality of first member ligands for binding to the target-binding ligands, thereby identifying one or more target-binding ligands,

(b) screening a second library comprising a plurality of second member ligands for the ability to inhibit the binding of one or more of said target-binding ligands to said target protein, thereby obtaining one or more inhibitory ligands, and

(c) determining which of the inhibitory ligands can mediate a biological activity of the target protein.

2. The method of claim 1 in which the first combinatorial library is composed of peptides and/or peptoids.

3. The method of claim 1 wherein the first combinatorial library is composed of nucleic acids.

4. The method of claim 1 in which the first combinatorial library is composed of peptides, peptoids and/or nucleic acids, and the second library is not.

5. The method of claim 1 in which the first combinatorial library has a greater diversity than the second library.

6. The method of claim 1 in which the second library is a combinatorial library.

7. The method of claim 1 in which the target-binding ligands obtained in step (a) are tested in a suitable biological system for the ability to interact with the target protein so as to mediate its biological activity and only the effective ligands are used in screening step (b).

8. The method of claim 1 in which the inhibitory ligands obtained in step (b) are tested to determine whether their inhibitory action is attributable to their binding the target

protein or to their binding the target-binding ligand.

9. The method of claim 1 in which the first library is a peptide library and the second library is a benzodiazepine library.

10. The method of claim 1 in which the first library is a biased peptide library, or a combination of two or more different biased peptide libraries, but not an unbiased peptide library.

11. The method of claim 1 in which the target protein is one associated with human cytomegalovirus.

12. The method of claim 11 in which the target protein is the DNA polymerase accessory protein UL44.

13. The method of claim 1 in which the target protein is an enzyme.

14. The method of claim 13 in which the target protein is a protein kinase.

15. The method of claim 13 in which the target protein is a transfer RNA synthetase.

16. The method of claim 13 in which the target protein is beta glucosidase, carboxypeptidase, or alcohol dehydrogenase.

17. The method of claim 1 in which the target protein is a transmembrane receptor.

18. The method of claim 1 in which the target protein is a nuclear receptor.

19. The method of claim 18 in which the target protein is an estrogen receptor.

20. Use of an inhibitory ligand identified by the method of ~~any of claims 1-19~~ claim 1 in the manufacture of a composition for the mediation of the biological activity of said target protein, provided that said inhibitory ligand was not previously known to mediate said biological activity of said target protein.

21. A structured panel of biased combinatorial peptide libraries, each library having one or two constant residues,

wherein, in each component library, at a first fixed position within the middle 50% of the peptide, the amino acid assigned to said first position is constant within said component library, is not the same in all libraries of said panel, and as a result of such library-to-library variation, said panel collectively presents all possible genetically encoded peptides of a predetermined length.

22. The panel of claim 21 wherein said peptides are of the form

$(Xaa)_m$-R1-$(Xaa)_n$,

where R1 is the amino acid at said first fixed position, and m and n do not differ by more than two.

23. The panel of claim 21, said structured panel further characterized in that in each library, a second position is held constant, but the location of said second position is varied so that said second position scans all residue position except for said first position, whereby the panel is composed of subpanels in which said first and second positions are fixed, and where, in each subpanel, the amino acid assigned to said second position is constant within said component library, but varies from library to library within said subpanel.

24. A biased combinatorial peptide library of the form

$(Xaa)_m$-Cys,

where m is greater than or equal to 5.